of the stratum corneum. These samples were then placed on modified Franz diffusion cells. The receptor was filled with 7.5 mL of 0.9% NaCl and 0.01% NaN_3 in deionized water. The cells were maintained at a constant 32° C. and were magnetically stirred at approximately 300 rpm. At specified time points, samples of the receptor phase were taken with complete replacement of the receptor phase. These samples were quantified by high-performance liquid chromatography (HPLC) utilizing Waters HPLC instrumentation. C-8 (15 cm×4.6 mm) 5 μm particle size columns (HYPERSIL made by MetaChem Technologies, Inc., Torrance, Calif.) were used at 50° C. (column temperature).

FIG. **1** illustrates the estradiol flux (μg/cm^2/hr) over time (0-81 hours) from transdermal delivery systems according to the invention (▲ & ●), as compared to Vivelle-Dot® (♦).

The results show that the systems according to the invention have a greater flux than the Vivelle-Dot® product and are able to achieve therapeutic daily dosages despite their significantly smaller size.

What is claimed is:

1. A monolithic transdermal drug delivery system for estradiol, comprising a single polymer matrix layer defining an active surface area and comprising a polymer matrix comprising estradiol as the only drug, wherein the polymer matrix layer has a coat weight selected from the group consisting of 12.5 mg/cm^2 and 15 mg/cm^2, includes greater than 0.156 mg/cm^2 estradiol, and achieves an estradiol flux that is greater than 0.01 mg/cm^2/day, based on the active surface area.

2. The transdermal drug delivery system of claim **1**, wherein the polymer matrix comprises a polymer blend comprising an acrylic adhesive, a silicone adhesive, and soluble polyvinylpyrrolidone (PVP).

3. The transdermal drug delivery system of claim **1**, wherein the polymer matrix comprises about 2-25% by weight acrylic adhesive, about 45-70% by weight silicone adhesive, about 2-25% by weight soluble PVP, and about 5-15% penetration enhancer, all based on the total dry weight of the polymer matrix.

4. The transdermal drug delivery system of claim **3**, wherein the penetration enhancer comprises oleyl alcohol.

5. The transdermal drug delivery system of claim **3**, wherein the penetration enhancer comprises dipropylene glycol.

6. The transdermal drug delivery system of claim **3**, wherein the penetration enhancer comprises oleyl alcohol and dipropylene glycol.

7. The transdermal drug delivery system of claim **3**, wherein the acrylic adhesive and silicone adhesive are present in a ratio of from about 1:2 to about 1:6, based on the total weight of the acrylic and silicone adhesives.

8. The transdermal drug delivery system of claim **1**, wherein the polymer matrix comprises an amount of estradiol effective to deliver a therapeutically effective amount of estradiol over a period of time selected from the group consisting of at least 1 day, at least 2 days, at least 3 days, at least 4 days, at least 5 days, at least 6 days and at least 7 days.

9. The transdermal drug delivery system of claim **1**, wherein the polymer matrix comprises an amount of estradiol effective to deliver an amount of estradiol selected from the group consisting of about 0.025, 0.0375, 0.05, 0.075 and 0.1 mg/day.

10. A monolithic transdermal drug delivery system for estradiol comprising a single polymer matrix layer comprising estradiol as the only drug, wherein the polymer matrix layer has a coat weight selected from the group consisting of 12.5 mg/cm^2 and 15 mg/cm^2, and the system has an active surface area that is about 60% of a size selected from the group consisting of 2.5, 3.75, 5.0, 7.5 and 10.0 cm^2 and is effective to deliver an amount of estradiol per day of about 0.025, 0.0375, 0.05, 0.075 and 0.1 mg/day, respectively.

11. A method for administering estradiol, con to the skin or mucosa of a subject in need thereof a monolithic transdermal drug delivery system comprising a single polymer matrix layer defining an active surface area and comprising a polymer matrix comprising estradiol as the only drug, wherein the polymer matrix layer has a coat weight selected from the group consisting of 12.5 mg/cm^2 and 15 mg/cm^2, includes greater than 0.156 mg/cm^2 estradiol, and achieves an estradiol flux that is greater than 0.01 mg/cm^2/day, based on the active surface area.

12. The method of claim **11**, wherein the system has an active surface area that is about 60% of a size selected from the group consisting of 2.5, 3.75, 5.0, 7.5 and 10.0 cm^2 and is effective to deliver an amount of estradiol per day of about 0.025, 0.0375, 0.05, 0.075 and 0.1 mg/day, respectively.

13. A method of making a monolithic transdermal drug delivery system for administering estradiol, comprising forming a polymer matrix comprising estradiol as the only drug and a polymer blend comprising an acrylic adhesive, a silicone adhesive, and soluble PVP, and applying the polymer matrix to a support layer to form a single polymer matrix layer such that the polymer matrix layer has a coat weight selected from the group consisting of 12.5 mg/cm^2 and 15 mg/cm^2 and includes greater than 0.156 mg/cm^2 estradiol.

14. The method of claim **13**, wherein the system has an active surface area that is about 60% of a size selected from the group consisting of 2.5, 3.75, 5.0, 7.5 and 10.0 cm^2.

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